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DOCKET NO.: ISIS-2297

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JAN 29 1990

At page 89, line 25, before "TTG CTT CCA TCT TCC TCG TC" please insert

--SEQ ID NO: 1--.

Remarks

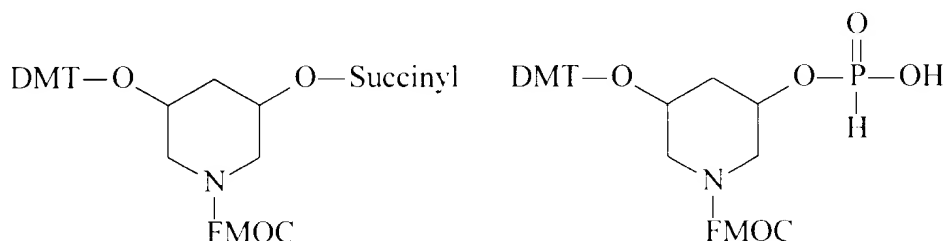
Applicants herewith submit a paper copy and computer readable format of the sequence listing. Applicants also attach hereto statements associated with the filing of sequence listings. Applicants note that the Office Action seems to suggest that there are references to sequences in the specification, other than the references cited on page 89, requiring incorporation into the sequence listing. Applicants have diligently searched the specification but have found none. Accordingly, only the sequence on page 89 is listed.

Claims 1-26 are pending in this application. Claims 1-26 stand rejected under 35 U.S.C. 112, first paragraph, for alleged lack of enablement. Applicants respectfully traverse the rejection, as the present claims are enabled within the patent laws.

The Office Action appears to base its assertion of nonenablement on the lack of a specific working example of the preparation of a nucleobase-bearing monomer of structure VI, stating that "nucleotide synthesis is well known in the art to proceed with detailed and complex protection and deprotection steps." However, the preparation of such monomers is not required to produce the oligomers of the present invention. Indeed, the present specification teaches the preparation of compounds of the invention by attaching a first aminodiol monomer having a protected hydroxyl and a protected amine site to a solid support (see for example Example 60 of

the specification), subsequent deblocking of the amine site, and then coupling to an activated group such as a carboxylated nucleobase (see for example Examples 62, 63 and 126 et seq. in the specification). The preparation of activated nucleobases useful for coupling to deprotected amine sites is shown in, for example, Examples 11-14. Further general procedures enabling the preparation of oligomeric compounds of the invention are illustrated in Examples 64-69.

With regard to compounds of structure VI, Example 77 on page 91 of the specification teaches the synthesis of (5R)-O-(t-butyldimethylsilyl)-(3R)-hydroxypiperidine from starting material N-benzyl-(5R)-O-(t-butyldimethylsilyl)-(3R)-hydroxypiperidine. Examples 78 through 80 teach the various protection and deprotection steps necessary to yield N-(Fmoc)-(3R)-O-Dimethoxytrityl-(5R)-hydroxypiperidine. Examples 81 and 82 teach the formation of compounds having structure VI such as the succinyl and H-phosphonates below:



Example 82

Example 81

Also, as stated above, guidance for attaching the aminodiol monomer subunit to a solid support also is disclosed in the specification at, for example, in Examples 82, 83, 60 and 61. Thus, the present specification provides more than enough guidance to demonstrate to one skilled

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in the art how to make and use the claimed compounds. Accordingly, the claims are fully enabled under the patent laws. Applicants therefore respectfully request that rejection be withdrawn.

The claims presently before the Examiner are believed to patentably define the invention over the prior art and otherwise be in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted.



Maureen S. Gibbons
Registration No. 44,121

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WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100